IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF PENNSYLVANIA

PFIZER, INC.,	)	
	)	
Plaintiff and	)	
Counterclaim Defendant,	)	
	)	
v.	)	02: 02cv1628
	)	
MYLAN LABORATORIES, INC. and	)	
MYLAN PHARMACEUTICALS, INC.,	)	
	)	
Defendants and	)	
Counterclaim Plaintiffs.	)	

FINDINGS OF FACT AND CONCLUSIONS OF LAW

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Order of Court

February 27, 2007

Pfizer Inc. filed this lawsuit against Defendants Mylan Laboratories, Inc., and Mylan Pharmaceuticals, Inc. for infringement of United States Patent Nos. 4,572,909 (the '909 patent) and Patent No. 4,879,303 (the '303 patent).[1] The parties tried this case on the '303 patent before the Court without a jury from November 28, 2006, through December 6, 2006. Following the trial, the parties filed Supplemental Proposed Findings of Fact and Conclusions of Law.

Based on the testimony and evidence presented during the bench trial and the applicable law, the Court finds that Defendants Mylan Laboratories, Inc., and Mylan Pharmaceuticals, Inc., have failed to prove by clear and convincing evidence that the '303 patent is invalid as obvious under 35 U.S.C. § 102. The Court also finds that Defendants have failed to prove by clear and convincing evidence that the '303 patent is unenforceable due to inequitable conduct before the United States Patent and Trademark Office ("PTO").

The Court now enters the following Findings of Fact and Conclusions of Law pursuant to Federal Rule of Civil Procedure 52(a):

FINDINGS OF FACT

I. The Parties and General Information

1. Plaintiff, Pfizer Inc. ("Pfizer"), is a corporation organized and existing under the laws of the State of Delaware. Pfizer has a principal place of business at 235 East 42nd Street, New York, New York. (*Stip. of Uncontested Facts ("Stip. Facts"), ¶ 1.*)

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[1] The '909 patent expired on July 31, 2006, and the claims relating to the '909 patent were dismissed by Order of Court on October 18, 2006.

2. Mylan Laboratories, Inc., is a corporation organized and existing under the laws of the Commonwealth of Pennsylvania and has its principal place of business at 1500 Corporate Drive, Canonsburg, Pennsylvania. (*Stip. Facts, ¶ 2.)*

3. Mylan Pharmaceuticals, Inc., is a corporation organized and existing under the laws of the State of West Virginia and has its principal place of business at 781 Chestnut Ridge Road, Morgantown, West Virginia. Mylan Pharmaceuticals, Inc. is a wholly-owned subsidiary of Mylan Laboratories, Inc.[2] *(Stip. Facts, ¶ 3.)*

4. The '909 patent, entitled "2-(Secondary Aminoalkoxymethyl) Dihydropyridine Derivatives as Anti-Ischaemic and Antihypertentive Agents," was issued by the PTO on February 25, 1986. The '909 patent covers a genus of compounds, including amlodipine, the active ingredient in Norvasc®. (*See '909 patent; MTX 1.)*

5. Simon F. Campbell, Peter E. Cross, and John K. Stubbs, are identified in the '909 patent as the inventors. Pfizer is identified as the owner of the '909 patent. *(Id.)*

6. The '303 patent, entitled "Pharmaceutically Acceptable Salts," was issued by the PTO on November 7, 1989. The '303 patent covers the besylate salt of amlodipine. *(Stip. Facts, ¶ 5.)*

7. Dr. James I. Wells ("Dr. Wells") and Mr. Edward Davison ("Mr. Davison") are identified in the '303 patent as the inventors. *(Stip. Facts, ¶ 7.)* Both Dr. Wells and Mr. Davison were employees of Pfizer in its Pharmaceutical Research & Development Group

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[2] The defendants, Mylan Laboratories, Inc. and Mylan Pharmaceuticals Inc., are hereinafter collectively referred to as "Mylan."

("Pharm. R&D") during the time that the tests described in the '303 patent were performed. *(Stip. Facts, ¶ 28.)*

8. Pfizer is identified as the owner of the '303 patent. *(See '303 patent, PTX 2 and MTX 2.)*

9. Mr. Keith Ruddock was the Pfizer in-house patent agent who oversaw the drafting and prosecution of the '303 patent. Mr. Ruddock was supervised by Dr. David Wood. James McManus was the Pfizer U.S. patent agent responsible for the prosecution of the '303 patent before the PTO. *(See Depo. of James McManus, Pfizer v. Mylan, at 99.)*

10. Typically, the Pfizer U.S. patent agents would not talk to the Pfizer U.K inventors before filing a U.S. patent application. *(See Depo. of James McManus, Pfizer v. Mylan, at 24.)* The U.S. patent agents would rely on the U.K patent lawyers or U.K patent agents to provide the information which needed to be submitted to the PTO. *(Id. at 34.)*

11. Pursuant to the provisions of 21 U.S.C. § 355a, the United States Food and Drug Administration ("FDA") granted Norvasc® a six-month period of pediatric exclusivity, which is applicable to the '303 patent. *(Stip. Facts, ¶ 9.)* The expiration date of the '303 patent is March 25, 2007, and the six-month period of pediatric exclusivity for the '303 patent, to the extent applicable, expires on September 25, 2007. *(Stip. Facts, ¶¶ 8, 10.)*

12. Pfizer filed a New Drug Application ("NDA") for Norvasc® (amlodipine besylate) tablets with the FDA on December 23, 1987. In the application, Pfizer advised the FDA that it had switched from maleate salt to besylate salt because the besylate salt had significantly better chemical stability and less sticking to processing equipment than the maleate salt. *(See Stip. Fact, ¶ 14.)*

13. The FDA approved Pfizer's NDA for amlodipine besylate tablets in late 1991. Thereafter, Pfizer proposed, and the FDA approved a four-year shelf life for amlodipine besylate tablets based on Pfizer's long-term stability data for the tablets. The current shelf life for Norvasc® tablets in bottles is 5 years. *(Stip. Facts, Trial Transcript V, at 2.)*

14. Norvasc® is approved by the FDA for treating hypertension and chronic stable and vasospastic angina. Norvasc® was launched as a commercial product by Pfizer in the United States in November 1992. *(See Stip. Facts, ¶¶ 15 and 54.)*

15. Pursuant to 21 U.S.C. § 355(b)(1) and the regulations of the FDA promulgated pursuant thereto, Pfizer listed the '909 patent and the '303 patent in the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book") as covering the drug substance, amlodipine besylate, in Norvasc®. *(Stip. Facts, ¶ 6.)*

16. On May 22, 2002, Mylan filed with the FDA an Abbreviated New Drug Application ("ANDA") No. 76-418, in which it sought approval to commercially sell 2.5 mg, 5 mg, and 10 mg dosage strength generic amlodipine besylate tablets (the "ANDA products"), before the expiration of the terms of the Pfizer '909 and '303 patents. *(Stip. Facts, ¶ 4.)*

17. By letter dated July 23, 2002, Mylan certified pursuant to 21 C.F.R. § 314.94(a)(12(i)A)(4) that it was seeking approval to market a generic version of Norvasc®.

18. Mylan has received final approval from the FDA of its ANDA No. 76-418, and plans to commercially sell the ANDA products in the United States, pursuant to 21 U.S.C. § 355(j)(2). *(Stip. Facts, ¶ 21.)*

19. On September 22, 2002, Pfizer commenced this patent infringement action against Mylan pursuant to 35 U.S.C. § 271(e)(2)(A), which makes it an act of infringement to file an ANDA for a drug claimed in a patent.

20. Pfizer seeks, *inter alia*, an order "permanently enjoining [Mylan]" from making, using, selling, offering to sell, or importing into the United States the Mylan Amlodipine Tablets described in ANDA No. 76-4618 until the expiration of the '909 patent term, . . . , and after the expiration of the '303 patent term . . . ."

21. The '909 patent expired on July 31, 2006. Thereafter, by Order of this Court dated October 18, 2006, the claims relating to the '909 patent were dismissed from this action for lack of subject matter jurisdiction.

22. Pfizer is asserting infringement only of claims 1, 2 and 3 of the '303 patent. Mylan does not contest infringement of these claims. However, Mylan alleges that claims 1, and 3 of the '303 patent are invalid under 35 U.S.C. § 103 as obvious and that the '303 patent is unenforceable for inequitable conduct before the PTO. (*See Stip. Facts, ¶ 22.)*

23. Claim 1 of the '303 patent is "[t]he besylate salt of amlodipine," which is generally known as "amlodipine besylate."

24. Claim 2 of the '303 patent is "[a] pharmaceutical composition comprising an anti-hypertensive, antiischaemic or angina-alleviating effective amount of the besylate salt of amlodipine as claimed in claim 1 together with a pharmaceutically acceptable diluent or carrier."

25. Claim 3 of the '303 patent is "[a] tablet formulation comprising anti-hypertensive, antiischaemic or angina-alleviating effective amount of the besylate salt of amlodipine as claimed in claim 1 in admixture with excipients."

26. If the Court holds that the '303 patent is valid and enforceable, the Mylan ANDA products, if manufactured, used, sold, or offered for sale in the United States, or imported for sale into the United States, will literally infringe claims 1, 2, and 3 of the '303 patent. *(Stip. Facts, ¶ 22.)*

II. Pharmaceutical Salts

27. A "base," such as amlodipine, is a compound which can become a positively charged ion. The positively charged ion of a base is called a "cation." An "acid" is a compound which can become a negatively charged ion. The negatively charged acid ion is called an "anion." *(Stip. Facts, ¶ 20.)*

28. A salt is the product of the reaction of a base and an acid. *(Stip. Facts, ¶ 19.)*

29. Acid addition salts may form as crystalline or amorphorous solids, or as liquids, such as oils. *(See Testimony of James I. Wells, Trial Transcript I, at 196.)*

30. A finished drug product consists of an active pharmaceutical ingredient together with inactive ingredients, known as excipients, in a dosage form such as a tablet, capsule, or injectable solution. *(See Testimony of Stephen W. Hoag, Trial Transcript V, at 165.)*

31. A pharmaceutically acceptable salt is any salt of an active drug molecule that can be used to make a finished drug product suitable for administration of the drug to a patient.

32. Pharmaceutical salts are evaluated for use in drug products based on their physicochemical or formulation properties which include aqueous solubility, chemical stability, hygroscopicity, and processability (*i.e.,* the ability to be manufactured into commercial dosage forms through the use of typical processing machinery).

33. The maximum amount of a compound that will dissolve at a specific temperature in a fixed amount of water, or water-based solvent, is called the aqueous solubility of the compound at that temperature. *(Stip. Fact, ¶ 23.)*

34. Pharmaceutical scientists, or formulators, use a rule of thumb for good solubility. Aqueous (in water or water-based solvent) solubility greater than 1 mg/ml at 37◦C is good solubility. *See '303 patent, Col. 2: 22-27.* Drug compounds having solubilities greater than the 1 mg/ml threshold or baseline generally have good bioavailability in oral dosage form.

35. Chemical stability relates to the resistence of a drug substance to chemically breakdown. Chemical stability may be determined for the drug substance alone ("bulk stability") or for the drug substance in combination with biologically inactive compounds known as excipients ("formulation stability"). *(Stip. Fact, ¶ 24.)*

36. The breakdown of the drug substance is known as degradation and the products from the breakdown of the drug substance are called "degradants." *(Stip. Fact, ¶ 25.)*

37. Chemical stability testing is also necessary to determine the shelf-life of the product.

38. Drug manufacturers assess chemical stability of an active drug compound alone and in admixture with excipients, *e.g.*, as the finished product.

39. Both the number and concentration of degradants in finished drug products are monitored closely as part of the drug development and approval process.

40. It is standard practice to use accelerated chemical stability testing in the pharmaceutical industry. Accelerated stability tests expose the active drug compound and finished product to high temperatures or high relative humidity in an effort to accelerate degradation that may occur over longer time periods at normal temperatures and relative humidities.

41. "Hygroscopicity," in the context of drug development, is a measure of the amount of water (moisture) that a drug compound absorbs when the drug compound is exposed to specified conditions of temperature, relative humidity, and time.

42. Hygroscopic drug compounds complicate the manufacturing process because precise measurement of the amount of active drug compound to be incorporated into a drug product is required. Absorption of moisture changes the weight of the active drug compound. Variation in the amount of the drug compound because of absorbed moisture may result in incorporating too little active drug into a drug product which will lead to variable dosing.

43. Nonhygroscopicity of a drug compound is also an important formulation property because absorbed water may promote chemical instability of a drug compound or drug product, or lead to changes in processability of the drug product.

44. "Processability" describes the ability of a formulation to be manipulated during the process of manufacturing a commercial dosage form, such as a tablet or capsule.

45. Stickiness, one aspect of processability, refers to adherence of the drug substance to the surfaces of manufacturing equipment, such as the metal surface of the punch face of a tablet press.

46. Stickiness is a problem when manufacturing a drug product because adherence of the drug substance to the surface of manufacturing equipment can interrupt production and/or cause a defective product to be made. In commercial tablet manufacturing very large quantities of tablets are produced on extremely high speed tablet presses. If a drug compound sticks to the punch faces of tablet presses while tablets are being made, the punch faces will require cleaning during tablet runs which would interrupt and slow production. Sticking to the punch face is referred to as "punch filming." Also, sticking may result in tablets having surfaces that are "picked" or pitted in appearance. *(See Testimony of Stephen W. Hoag, Trial Transcript V, at 170-78.)*

47. Manufacturing deficiencies, such as sticking, when observed in small experimental tablet operations will be more significant when using extremely high speed tablet presses. For that reason, pharmaceutical formulators strive to achieve "robust" tablet formulations, *i.e.,* formulations that can be tableted without production problems in a variety of conditions.

48. Pharmaceutically acceptable salts are those which are non-toxic and have no significant impurities or degradation products formed as a result of chemical breakdown of the salt, alone or in combination with excipients, over extended time periods, and which are suitable for making a dosage form that is administrable to a patient. The term

"pharmaceutically acceptable salt" does not convey any information about a particular salt or its chemical structure.

III. Amlodipine and Amlodipine Maleate

49. Amlodipine is the common name for the chemical compound 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-3-ethoxycarbonyl-5-methoxycarbonyl-6-methyl-1,4-dihydropyridine, which is a member of the class of compounds referred to as "1,4-dihydropyridines." *(Stip. Fact, ¶ 16.)*

50. Amlodipine is a biologically active chemical compound that has anti-hypertensive and anti-ischaemic activity in the body. *(Stip. Fact, ¶ 26.)* Anti-hypertensive activity means that amlodipine lowers the blood pressure of a patient. Antiischaemic activity means that amlodipine reduces angina, the pain associated with a lack of blood flow to the heart muscle.

51. Amlodipine maleate is an acid addition salt, formed from the reaction of amlodipine and maleic acid. *(Stip. Fact, ¶ 27.)*

52. During the 1980's, each new active moiety made at Pfizer's Sandwich, England research facility was assigned a code beginning with the prefix "UK", for the United Kingdom, followed by a five-digit number. *(Stip. Fact, ¶ 29.)*

53. Amlodipine was assigned compound number "UK-48,340." *(Stip. Fact, ¶ 30.)*

54. During the 1980's, salts made from a particular acid anion were assigned a code by Pfizer which consisted of the code for the active moiety followed by a two-digit or two-letter code used for all salts made from that acid anion. *(Stip. Fact, ¶ 31.)*

55. The Pfizer two-digit code for the maleate anion was "11," and amlodipine maleate was assigned code "UK-48,340-11." *(Stip. Fact, ¶ 32.)*

56. The two-digit Pfizer codes for the anions listed in the '303 patent are as follows: Hydrochloride anion was "01"; Acetate anion was "14"; Tosylate anion was "15"; Succinate anion was "24"; Besylate anion was "26"; Mesylate anion was "27"; Lactate anion was "50"; Salicylate anion was "AB." *(Stip. Fact, ¶¶ 33-40.)*

57. On or about July 14, 1982, the Pfizer Discovery Chemistry Group located at the Pfizer Central Research Laboratories in Sandwich, England, recommended that an effort be made to develop amlodipine into a commercial product. Clinical studies on amlodipine maleate were planned for 1983.

58. The finished commercial product was intended to be an 20 mg amlodipine maleate tablet. *(See Deposition of Edward Davison, Pfizer v. Apotex, at 128; Deposition of Edward Davison, Pfizer v. Synthon, at 38.)* Tablets are the preferred oral dosage form for several reasons, which include patient acceptance, self-administration, and tablets are the optimum economic commercial dosage form to manufacture. *(Id.; See Testimony of Stephen W. Hoag, Trial Transcript V, at 179.)*

59. In 1982, the Pfizer Pharm. R&D Group, also located in Sandwich, England, was responsible for developing commercial dosage forms (drug products) of pharmacologically active compounds discovered and recommended by the Pfizer Discovery Chemistry Group.

60. Neither Dr. Wells nor anyone in Pharm. R&D participated in selecting amlodipine maleate as the amlodipine salt to be developed to a commercial dosage form. The salt form was selected by the Discovery Chemistry Group. *(See Testimony of James I. Wells, Trial Transcript I, at 189; see also Deposition of Edward Davison, Pfizer v. Apotex, at 5.)*

61. In 1982, the head of Pharm. R&D was Mr. J.E. Jeffries. His deputy, Dr. J.R. Davidson, assigned Dr. Wells, a group development leader in Pharm. R&D, the primary responsibility to develop a commercial tablet formulation of amlodipine maleate. *(See Testimony of James I. Wells, Trial Transcript I, at 192.)*

62. Dr. Wells assigned Mr. Davison, a physical chemist within Pharm. R&D,[3] to assist him in developing the formulation properties of amlodipine maleate. Ms. Teresa Cutt, Mr. David Smith, and Ms. Sally Darling, also members of the Pharm. R&D, were also assigned to the project of developing a commercial amlodipine maleate tablet.

63. At the time that Dr. Wells and Mr. Davison were given this assignment, neither scientist expected that formulating a commercial dosage form of amlodipine maleate would present any problem in terms of stability or processability. It did not occur to Dr. Wells that the amlodipine and the amlodipine maleic acid would react and produce a degradation problem. *(See Testimony of James I. Wells, Trial Transcript I, at 197.)*

64. Dr. Wells and Mr. Davison worked closely with the Pfizer Process Research & Development Group ("Process R&D") and the Analytical Chemistry Department.

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[3] Mr. Davison received his Bachelor of Science in chemistry and physics. *See Deposition of Edward Davison, Pfizer v. Apotex, at 2.*

65. Dr. Wells decided that amlodipine maleate tablets should be manufactured using the direct compression process. *(Id. at 194.)*

66. "Direct compression" is a method of tablet making which is desirable for manufacturing purposes on a commercial scale because it has fewer processing steps, reduces the potential for hydrolytic breakdown, and is more cost effective than other tablet manufacturing processes. (*See Testimony of Stephen W. Hoag, Trial Transcript V, at 179.)* Water or other liquid excipients are not used in the direct compression process. *(Id. at 179-81).*

67. In the mid-1980's, as today, "direct compression" tablet manufacturing was the method of choice when the active drug compound in the finished drug product is less than about twenty-five per cent (25%) of the total tablet weight or when hydrolytic instability of the active drug compound is a concern. **(***Id.*)

68. Amlodipine maleate was stable in bulk form (*i.e.,* before being mixed with excipients and processed into a useable dosage form.) However, when Dr. Wells and Mr. Davison began trying to formulate a direct compression amlodipine maleate tablet, they discovered two significant and interrelated problems: (i) the sticking of the amlodipine maleate salt to the metal punch face of the tablet making press and (ii) the chemical instability of the amlodipine maleate salt.

69. The sticking problem became exacerbated when tablets were made on a high speed commercial production press. *(See Testimony of James I. Wells, Trial Transcript I, at 216.)*

70. Toward the end of 1983, Pfizer's Analytical Chemistry Department "diagnosed" that the instability of the amlodipine maleate was caused by the Michael Addition

Reaction ("MAR"), which was generating two percent (2%) of a new degradant compound identified as UK-57,269 in the maleate formulations. *(Id. at 164, 216; see also Testimony of Robin V. Platt, Trial Transcript V, at 4; see also Deposition of Edward Davison, Pfizer v. Apotex, at 37.)* Two percent (2%) of the MAR compound was not acceptable to Dr. Wells for a commercial product. *(See Testimony of James I. Wells, Trial Transcript I, at 223).* Dr. Robin Platt ("Dr. Platt"), a member of Pfizer's Analytical Chemistry Department, was assigned the responsibility for testing the stability of amlodipine maleate in tablet and capsule formulations. He discovered that in the capsule formulation, the degradation of amlodipine maleate was dominated by one main degradation product, UK-57,269. (*See Testimony of Robin V. Platt, Trial Transcript V, at 24.)*

71. Dr. Platt also discovered that in the amlodipine maleate tablet formulation the pattern of degradation was more complex in that degradation products included not only the formation of UK-57,269, but at least another ten unknown degradation products were also produced. *(Id.; see PTX 120 at P0177100-102.)*

72. Initially, Dr. Wells speculated that the ten unknown degradation products may be derivatives of UK-57,269 *(see PTX 123 at P0187936-7)*; however, it was ultimately determined that those unknown degradants in the amlodipine maleate tablet formulations were not by-products of the degradant UK-57,269. *(PTX 284 at P0190403-4; Trial Tr. December 4, 2006 at 42: 1-17.)*

73. The development of the MAR in the capsule and tablet formulations of amlodipine maleate was not expected. *(Trial Tr. December 4, 2006 at 33:6-11).* It could not have been predicted from the structures of the amlodipine and maleic acid molecules. The

Pfizer Discovery chemists, who were skilled synthetic organic chemists, knew about the MAR generally, i.e., as an abstract reaction such as oxidation. Nevertheless, they designated the amlodipine maleate salt as the development candidate. Had the Pfizer Discovery chemists expected that amlodipine maleate, in formulation, would undergo a MAR, they would not have designated that salt as the development candidate. *(Id. at 34:25-37.9.)*

74. A synthetic organic chemist would not expect the MAR to occur in solid state formulations of amlodipine maleate, but would have expected the reaction to occur only in solution at high temperature. Additionally, he or she would not have expected that a neutral (uncharged) primary amine (NH_2) must be present for a MAR to occur. *(Trial. Tr., Dec. 5, 2006 at 143:12-146:3.)*

75. The conditions that one of ordinary skill would have expected to be necessary for a MAR are not present in a solid state formulation of amlodipine maleate. The primary amine is present as a nonreactive cation, i.e., a positively charged species (NH_3+) and not a reactive neutral species (NH_2). The amlodipine cation and maleate anion are locked in place in the crystal lattice, not free to move and reorient themselves to participate in a MAR.

76. The references Dr. Burgess identified which describe a MAR between a primary amine and maleic acid teach reaction conditions that are vastly different from those in a solid state formulation of amlodipine maleate. The conditions taught require putting the reactants in solution at high temperatures, boiling water, for example, for long periods of time, in the presence of excess amine or the addition of base to make the solution alkaline. None of these conditions is present in a solid state formulation of amlodipine besylate, and those

references would not have been ones that a person of ordinary skill would have considered in attempting to make a tablet of an amlodipine salt. *(Id. at 146:12-147:22.)*

77. Just as it had not been predicted by the Pfizer Discovery chemists, the MAR was not predicted by Pfizer analytical or process chemists. It was identified only by hindsight after the UK-57,269 degradant had been isolated and its chemical structure had been determined by sophisticated analytical techniques. From the chemical structure of UK-57,269, Pfizer chemists, after months of investigation, were able to determine that a MAR had caused the degradant to be formed. *(Trial Tr., Nov. 28, 2006 at 223: 12-225:11.)*

78. Dr. Burgess pointed to a statement in a quarterly report of ACD in May 1985 and the fact that a MAR cannot occur in amlodipine besylate - the besylate anion has no carbon double bond - as evidence that the MAR was predictable from the structure of amlodipine. The statement, referring to a comparative stability study of amlodipine besylate and maleate tablets, is: "As expected the besylate demonstrated a superior stability profile over the maleate." The stated expectation has nothing to do with the MAR. The expected superiority of the amlodipine besylate salt is based not on the absence of a MAR, but on the stability study that had been conducted by Pfizer. During the second half of 1984, Dr. Platt had extensively studied the stabilities of amlodipine salts and he had concluded that the besylate salt in formulation is significantly more stable than the maleate salt. Accordingly, the May 1985 report states that the same result in the follow-up comparative tablet study was expected. *(Trial Tr., Dec. 4, 2006 at 98:4 - 101: 25.)*

79. Dr. Wells and Mr. Davison's first strategy to control the sticking and instability of amlodipine maleate was to change the excipients in the formulations. The fact

that the sticking and instability problems were interrelated, *i.e.*, excipients that reduced sticking exacerbated instability and increased the difficulty of finding a formulation that controlled the problems exhibited by the maleate salt of amlodipine.

80. Amlodipine maleate was also discovered to be very unstable in a liquid formulation and required the addition of cosolvents in order to increase stability. *(See Testimony of James I. Wells, Trial Transcript I, at 225-26.)*

81. As a result of these difficulties, Dr. Wells became concerned that he could not produce a commercially viable direct compression amlodipine maleate tablet formulation. On April 24, 1984, Dr. Wells proposed to Dr. Davidson, his supervisor and the head of Pharm. R&D, that other salts of amlodipine be considered for development and as replacements for amlodipine maleate. Dr. Wells identified several acids which could be used to attempt to make a new salt for testing. *(See PTX 123 / MTX 293; Testimony of James I. Wells, Trial Transcript I, at 231.)*

82. Dr. Wells predicted that amlodipine acetate and amlodipine free base[4] would have the greatest likelihood to overcome the instability problems exhibited by amlodipine maleate. These predictions turned out to be wrong, as both amlodipine acetate and amlodipine free base were much more unstable than amlodipine maleate. (*See Testimony of Robin V. Platt, Trial Transcript V, at 44.)*

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[4] Amlodipine base or amlodipine free base refers to the amlodipine molecule alone without reaction with an acidic molecule.

83. Dr. Wells also stated in his memorandum that if management was unwilling to consider making and testing new amlodipine salts, then a different 1,4-DHP compound than amlodipine should be considered for development. *(See PTX 123.)*

84. Dr. Platt expressed reservations about Dr. Wells' proposal to try to find a new amlodipine salt because of the potential high risk of failure. *(See PTX 120; Memorandum from R. V. Platt to P. F. Wadsworth, dated May 3, 1984; see also Testimony of Robin V. Platt, Trial Transcript V, at 51, 80.)* He cautioned that new salts of amlodipine would not necessarily have better stability than amlodipine maleate, as each acid could result in a salt with its own unique degradation pathways or other problems. (*See Testimony of Robin V. Platt, Trial Transcript V, at 26-27.)*

85. At the time Dr. Wells made his proposal, the amlodipine maleate salt, in the form of capsules and intravenous injections, was being tested by Pfizer on human beings in clinical trials. *(Stip. Fact, ¶ 41.)*

86. Soon after Dr. Wells' April 24, 1984 recommendation was approved, he asked Pfizer's Process R&D scientists to attempt to make new acid addition salts of amlodipine. Process R&D created the following salts, based upon the acids that Pfizer had on hand at the time: amlodipine besylate, amlodipine tosylate, amlodipine mesylate, amlodipine succinate, amlodipine salicylate, amlodipine acetate, amlodipine hydrochloride, and amlodipine naphthsylate. *(See Testimony of Robin V. Platt, Trial Transcript V, at 54; see also PTX 75.)*

87. Dr. Wells also requested that Process R&D try to make additional amlodipine salts that he identified in order to test their physicochemical properties and compare those properties with amlodipine maleate. All of the salts selected by Dr. Wells had previously been

used in pharmaceutical formulations. *(See Testimony of James I. Wells, Trial Transcript I, at 175.)*

88. Dr. Wells chose these candidates from a larger number of pharmaceutically acceptable acids of which he was aware from various sources. However, he could not predict whether any particular salt of amlodipine would form as a crystalline salt, or what the physicochemical properties would be of any salts that did form. Dr. Wells proposed a broad range of salts, including sulfonates, carboxylates, and inorganic salts. *(See Testimony of James I. Wells, Trial Transcript I, at 176, 178; see also Testimony of Robin V. Platt, Trial Transcript V, at 75.)*

89. Dr. Wells did not know prior to testing whether any salt which he proposed would be an improvement over amlodipine maleate. However, Dr. Wells had "high hopes" that besylate would be a possible alternative to the maleate. *(See Testimony of James I. Wells, Trial Transcript I, at 176, 178.)*

90. Dr. Platt did not know prior to testing whether any salt proposed by Dr. Wells would be an improvement over amlodipine maleate. *(See Testimony of Robin V. Platt, Trial Transcript V, at 49.)*

91. Dr. Wells and Mr. Davison, together with other members of Pharm R&D and Dr. Platt, established testing protocols and tested the new amlodipine salts made by Process R&D for the physicochemical properties of solubility, hygroscopicity, chemical stability in formulations, and processability, *i.e.*, sticking to the tablet-making equipment. Amlodipine maleate, which exhibited unacceptable sticking and stability, was used as the control in the experiments. **(***See Testimony of Robin V. Platt, Trial Transcript V, at 62.)*

92. Pfizer scientists used methods routinely employed by Pfizer and the pharmaceutical industry in general to test the new amlodipine salts for solubility, hygroscopicity, and instability. For sticking, Mr. Davison adapted a test previously used by another member of Pharm R&D to measure sticking of a different active compound.

Solubility Findings

93. The aqueous solubility of amlodipine besylate, as well as all of the other new amlodipine salts, was tested and measured. All of the new amlodipine salts, except amlodipine tosylate, had solubilities above the 1 mg/ml threshold preferred by formulation scientists. The new salts were not rank-ordered according to their solubility values. None of the new amlodipine salts was eliminated from consideration based on solubility testing.

94. The solubility of each new batch of salt that Process R&D made was measured. Multiple batches were made and the solubility of each batch, along with the original development candidate, amlodipine maleate, and the eventual commercial product, amlodipine besylate, were measured.

95. The solubility of the amlodipine besylate fell in the mid-range of solubilities of the amlodipine salts tested. *(See '303 patent, col. 2, Table 1.)*

96. The solubility value for amlodipine besylate reported in the '303 patent, 4.6 mg/ml, is consistent with the aqueous solubility that Pfizer's formulation scientists measured for amlodipine besylate in an experiment conducted in September 1985. That experiment, in which a pH/solubility profile for amlodipine besylate was produced, reports that the solubility of amlodipine besylate is between 4.6 and 4.7 mg/ml over a range of pH values from 1 to 7. *(PTX 635 at P0056829-30; Trial Tr., Dec. 5, 2006 at 169:1 - 172:10.)* The experiment was

carried out just two months before Dr. Wells submitted to the Pfizer patent department in Sandwich, the invention disclosure that became the '303 patent application. *(PTX 611 at P0085952.)* Moreover, the tosylate solubility value that is set out in the patent, 0.9 mg/ml, is recorded in the very next experiment in the same laboratory notebook. *(PTX 635 at P0056831.)*

97. There are different aqueous solubility values reported for amlodipine besylate in other Pfizer documents prepared during the development of amlodipine tablets. In Dr. Wells' October 11, 1984 memo to Dr. Davidson, he reports a solubility value of 3.6 mg/ml for amlodipine besylate. *(PTX 76 at P0152406.)*

98. Solubility values can vary from batch to batch based on any number of variables in experimentation as reflected in the above referenced finding. Such variations are not unexpected and do not mean that one or the other is incorrect. The '303 patent states that any solubility greater than 1 mg/ml is acceptable and, therefore, the difference between 3.6 mg/ml and 4.6 mg/ml is immaterial under the circumstances.

99. The solubility of the amlodipine besylate could not have been predicted; it had to be made and tested. *(See Testimony of Robin V. Platt, Trial Transcript V, at 72.)*

Hygroscopicity Findings

100. Mr. Davison and members of the Pharm. R&D tested all of the newly created amlodipine salts for hygroscopicity, which was measured by subjecting each of the amlodipine salts to controlled temperatures, relative humidity, and time conditions that may be encountered during the manufacturing, storage, or transportation processes, *e.g.*, 75% relative humidity ("RH") at 37◦ for 24 hours, and 95% RH at 30◦ for three days.

101. Amlodipine besylate, amlodipine tosylate, and amlodipine maleate were the only amlodipine salts that were nonhygroscopic at 75% RH and 37◦ for 24 hours. Amlodipine besylate and amlodipine maleate were the only amlodipine salts that were nonhygroscopic at 95% RH and 30◦ for three days. With the exception of the besylate salt and the maleate salt, all of the amlodipine salts that were tested proved to be hygroscopic at test conditions. All of the sulfonic acid salts other than besylate that were tested were hygroscopic.

102. The fact that the besylate salt of amlodipine was capable of remaining nonhygroscopic through the range of conditions used in the tests could not have been predicted.

Formulation Stability Findings

103. To determine formulation stability, Mr. Davison and other members of the Pharm. R&D, as well as Dr. Platt, had to test all of the newly created amlodipine salts. Multiple formulation blends of each of the newly created amlodipine salts, with different excipients, were made and tested. Tablets were also made by compressing some of the blends.

104. For testing purposes, the tablets were exposed to a range of elevated temperatures to promote degradation. Dr. Platt used the analytical procedure known as thin-layer chromatography ("TLC") to measure the chemical stability of multiple blends and tablets which contained amlodipine salts at multiple time intervals after they had been stored at a fixed temperature. *(See Testimony of Robin V. Platt, Trial Transcript I, at 16-20.)* TLC was a well accepted technique in the pharmaceutical industry for studying the chemical stability of drug compounds. It also was the standard analytical method which he used at Pfizer for stability testing of new compounds, and it was suitable to rank order the tested amlodipine salts based on their respective stabilities.

105. Dr. Platt measured the chemical stabilities of the new amlodipine salts and amlodipine free base, and the amlodipine maleate salt in multiple blends and compacts at multiple time intervals after they had been stored at controlled temperatures. He used multiple solvent systems in the TLC analysis to assure that all degradants would be detected.

106. Dr. Platt evaluated the number and relative amounts of degradants produced by each amlodipine salt in each of the multiple formulations after exposing each blend of each amlodipine salt to accelerated temperature.

107. Dr. Platt discovered that the various newly created amlodipine salts degraded at different rates and produced different kinds and amounts of degradation products when exposed to a range of temperatures and measured at different times.

108. Dr. Platt used amlodipine maleate as a control in these experiments. Amlodipine maleate degraded in formulation to create the degradant UK-57,269, a product caused by the "MAR" of the amlodipine ion interacting with the maleic acid ion.

109. Based on chemical stability data which he accumulated, on October 9, 1984, Dr. Platt prepared a rank ordering of all the amlodipine salts he tested. *(Stip. Fact, ¶ 43; PTX 75)*. Dr. Platt concluded that amlodipine besylate was the most stable in formulation of all of the amlodipine salts that he had tested. Based on the rank order, it also appeared to Dr. Wells that amlodipine besylate was the best choice for an alternative to amlodipine maleate. *(See Testimony of James I. Wells, Trial Transcript II, at 3.)*

110. Despite the fact that acetic acid and hydrochloric acid could not undergo a MAR, the salts made from those acids exhibited significantly worse formulation stability than

amlodipine maleate. Amlodipine free base, which also could not undergo a MAR, had significantly worse stability in formulation than amlodipine maleate.

111. The formulation stability of the besylate salt of amlodipine was not expected and could not have been predicted either from the elimination of the MAR or otherwise. *(See Trial Transcript; December 4, 2006 at 48: 25 - 50: 7.)*

Processability Findings

112. In 1984, Mr. Davison designed and developed a study to compare the punch filming properties of each of the newly created amlodipine salts to measure sticking by making tablets with blends of the salts and measuring the amount of amlodipine that adhered to the tablet punch face as a function of the number of tablets made. *(See '303 patent, col. 3, Lines 50 - 65; PTX 76 at P0152404.)*

113. Mr. Davison tested the amlodipine salts for sticking by making tablets of the different amlodipine salts in the same tablet formulation. The principal excipient of the formulation was calcium dihydrate (Compactrol®) and it also included the lubricant magnesium stearate, at one percent (1%) of the weight of the formulation. The amlodipine maleate salt was again used as the control in the sticking experiments.

114. The sticking studies measured the rate at which amlodipine stuck to the tablet punch face. Mr. Davison measured the rate of sticking for each salt by calculating the slope of the best-fit straight line for a plot of amount of salt per unit area stuck to the punch face against number of tablets made.

115. Mr. Davison's studies were well designed, controlled, and properly carried out.

116. These tests demonstrated that the amlodipine besylate was forty-one percent (41 %) less sticky than amlodipine maleate. The tests also showed that amlodipine besylate was less sticky than all but one of the other amlodipine salts, the amlodipine mesylate, which was forty-two percent (42%) less sticky than amlodipine maleate.

117. To confirm his results with the Compactrol® formulation, Mr. Davison also did a head-to-head study of only amlodipine besylate and amlodipine maleate in the then-lead tablet formulation, known as FID 0650. The principal ingredients of each of the formulations were microcrystalline cellulose (Avicel®) and anhydrous dibasic calcium phosphate with the lubricant magnesium stearate at one percent (1%) of the total weight of the formulation. The study confirmed that on longer runs of tablets, amlodipine besylate was significantly less sticky than amlodipine maleate.[5]

118. Based on all the test results of the amlodipine salts, Dr. Wells concluded that the besylate salt had a combination of outstanding formulation properties.

119. The fact that one salt would have outstanding properties in all of the categories tested could not have been predicted.

120. On or about October 11, 1984, Dr. Wells recommended to Dr. J. R. Davidson, the head of Pharm. R&D, that the amlodipine besylate salt be substituted for the

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[5] The decreased stickiness of amlodipine besylate was also demonstrated by amlodipine besylate scale-up studies carried out by Ms. Teresa Cutt in 1985, after Mr. Davison had determined that besylate was significantly less sticky than maleate.

amlodipine maleate salt in the commercial amlodipine tablet product. *(Stip. Fact, ¶ 44; MTX 310.)*

121. At the time Dr. Wells made his recommendation to switch salts, Pfizer was conducting Phase II clinical trials of amlodipine maleate (using capsules and intravenous injections). *(Stip. Fact, ¶ 45.)*

122. Dr. Wells' recommendation to switch salts late in the development cycle, while Phase II clinical trials were underway, was very unusual and a direct result of the seriousness of the chemical instability and sticking problems that Pharm R&D had experienced in attempting to develop a direct compression commercial tablet formulation of amlodipine maleate.

123. Based on the test results of Wells, Platt, and Davison, Pfizer's senior research and development management decided to switch from amlodipine maleate to amlodipine besylate for the direct compression amlodipine commercial tablet.

124. At the time Pfizer senior research and development management decided to switch salts, Pfizer had begun Phase II clinical trials of amlodipine maleate. Switching salt forms of a drug candidate in the Phase II clinical trial phase was unprecedented at Pfizer.

125. Pfizer filed an amended Investigatory New Drug ("IND") application with the FDA which reflected a switch in salts from amlodipine maleate to amlodipine besylate on or about May 5, 1986. Pfizer submitted additional test data to the FDA for the besylate salt with its amendment. (*Stip. Fact, ¶ 46.)*

126. On or about November 25, 1985, more than a year after he recommended switching salts from amlodipine maleate to amlodipine besylate, Dr. Wells submitted to

Pfizer's patent group in Sandwich, England, the invention disclosure that led to the preparation and filing of the '303 patent and its foreign counterparts. *(See Stip. Fact, ¶ 47.)*

IV. The Discovery of Amlodipine Besylate

127. Amlodipine besylate is an acid addition salt, formed from the reaction of the chemical base amlodipine and benzene sulphonic acid. *(Stip. Fact, ¶ 18.)*

128. After Pfizer switched to amlodipine besylate, it took only three efforts to solve the problems associated with maleate. Pharm R&D was able to produce a chemical size batch within a year of the switch. *(See Testimony of James I. Wells, Trial Transcript II, at 7.)*

129. Dr. Wells' preference is to use one-half percent (0.5%) of lubricant in a formulation; however with the amlodipine besylate formulation he chose to use one percent (1%) because of an "extreme sticking problem" which he had with maleate, "but we had clearly improved with the besylate . . . one percent was a sensible position . . . [i]t left us with a margin of safety." *(Id.)*

130. Since 1997, Norvasc® has been the largest selling branded cardiovascular drug product in the world.

131. In 2003, Norvasc® sales in the United States exceeded $2.1 billion. *(Stip. Fact, ¶ 56.)*

132. The worldwide sales of Pfizer's amlodipine besylate drug product are approximately $4 billion annually. *(Stip. Fact, ¶ 57.)*

133. Pfizer's amlodipine besylate drug product is its second-largest selling product in terms of worldwide annual dollar sales. *(Stip. Fact, ¶ 58.)*

V. The '303 Patent Prosecution

A. The '303 Patent Application

134. On April 4, 1986, Pfizer filed its first patent application in which it claimed amlodipine besylate, British Patent Application No. 8,608,335 (the " British priority application"). *(Stip. Fact, ¶ 13.)* The British priority application was filed almost two years after Dr. Wells had first recommended making and testing new amlodipine salts (April 24, 1984) and approximately 1-½ years after he recommended switching the amlodipine salt from maleate to besylate (October 11, 1984).

135. The '303 patent issued from the United States Patent Application Serial No. 256,938 (the " '938 application"), which was filed in the PTO on October 13, 1988. *(Stip. Fact, ¶ 11.)*

136. The '938 application is a continuation of United States Patent Application Serial No. 30,658 (the " '658 application"), which was filed in the PTO on March 25, 1987. *(Stip. Fact, ¶ 12.)*

137. Pursuant to 35 U.S.C. § 119, the '303 patent claims, and is entitled to, priority based on the April 4, 1986 filing date of the British priority application. *(Stip. Fact, ¶ 13.)*

138. In an Office Action dated October 6, 1987, the PTO examiner found Pfizer's claims to amlodipine besylate to be unpatentable and rejected them as *prima facie* obvious under 35 U.S.C. § 103 over Pfizer's earlier '909 patent on amlodipine and two prior art patents - the Schmidt patent and the Spiegel patent.

139. The PTO Examiner rejected the '658 application as *prima facie* obvious three separate times. On June 17, 1988, the PTO Examiner issued a final rejection.

140. The '303 patent applicants let their patent application go abandoned and filed a continuation application (the ' 938 application) on October 13, 1988, pursuant to 35 U.S.C. § 103.

141. Along with the '938 application, Pfizer submitted to the PTO a Preliminary Amendment of the claims and the Declaration of Dr. Wells dated October 3, 1988 (the "Wells Declaration"), in support of the patentability of the claims in the '938 application. *(See MTX 435.)* The Wells Declaration opines regarding the four characteristics of an active ingredient that are relevant to whether the active ingredient can be made into a pharmaceutical formulation. *(See Depo. of James McManus, Pfizer v. Mylan, at 105.)*

142. The Wells Declaration was submitted under 37 C.F.R. § 1.132 and the declarant, Dr. Wells, swore that the statements made therein were true. (*See MTX 436.*)

143. On November 7, 1989, the Patent Examiner allowed the claims of the '938 application. She did not state whether, in allowing the claims, she had relied on the data in the Wells Declaration which demonstrated amlodipine besylate's unexpected combination of advantageous formulation properties or the arguments of the Pfizer patent attorney that there was no *prima facie* case of obviousness.

144. On November 7, 1989, the PTO issued the '303 patent.

B. Obviousness

i. The Scope and Content of the Prior Art

145. It is undisputed that the following references are prior art to the '303 patent: the '909 patent; a publication by Berge, S.M., et al, "Pharmaceutical Salts," (Jan. 1977) *J.*

Pharm. Sci. 66:1-19 ("Berge"); United States Patent No. 4,432,987 ("Barth"); United States Patent No. 3,816,612 (1974) ("Schmidt"); United States Patent No. 4,032,637 (1977) ("Spiegel"); United States Patent No. 4,346,099 (1982) ("Tanouchi"); United States Patent No. 3,982,007 (1976) ("Laber"), as well as other references are prior art to claims 1 through 3 of the '303 patent. *(Stip. Fact, ¶ 48.)* The Berge, Speigel, and Schmidt references were before the PTO during the prosecution of the '303 patent.

146. Pfizer internal memoranda which relate to its own development of amlodipine maleate and its having identified, made, and tested new amlodipine salts are not prior art to the '303 patent.

147. The compound amlodipine is described in the prior art to the '303 patent. *(Stip. Fact, ¶ 49.)*

148. The '909 patent issued on February 25, 1986. At the time the '909 patent issued, the patent term was seventeen (17) years from the date of issuance.

149. The '909 patent contains a specific claim (claim 8) to amlodipine.

150. The '909 patent identifies maleic acid as the preferred acid used to form salts (maleate salts) with the compounds disclosed and claimed by the patent. The only salt of amlodipine described in the '909 patent is amlodipine maleate. No information concerning the solubility, hygroscopicity, stability, or processability of amlodipine maleate is provided in the '909 patent. *(See '909 Patent, MTX 1.)*

151. The '909 patent recites twelve (12) acid anions that may be combined with the '909 claimed compounds in order to try to make pharmaceutically acceptable acid addition

salts. Neither benzene sulphonic acid, nor any other sulphonic acid, is identified, disclosed, or mentioned in any way in the '909 patent.

152. The '909 patent teaches that amlodipine salts are useful for treating high blood pressure and preventing a variety of heart conditions including angina pectoris, cardiac arrhythmia, heart attack, cardiac hypertrophy, and coronary vasospasm.

153. The Berge article sets the tone for the theme that the properties of salt(s) are unpredictable. ("Choosing the appropriate salt, however, can be a very difficult task, since each salt imparts unique properties to the parent compound." Berge, at 1.) (*See PTX 266*; *Testimony of Bradley Anderson, Trial Transcript VI, at 113 - 14.)*

154. The Schmidt patent teaches that aryl sulfonic acid salts improve the solubility of nitrogen-containing pharmaceutical compounds and, thus, are preferred over other salts. Benzene sulfonic acids are identified as "especially suited examples of such sulfonic acids." (*See PTX 511 / MTX 81.)*

155. The Speigel patent describes the use of mesoridazine as a sleep promoting agent, *(See Testimony of Bradley Anderson, Trial Transcript VI, at 119),* and teaches that the preferred pharmaceutically acceptable acid-addition salt is besylate. *(See PTX 513.)*

156. The Tanouchi patent refers to carboxy-imidazole derivatives and uses for treating patients for diseases caused by thromboxane A2. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 133-34; PTX 514.)*

157. The Tanouchi patent teaches that certain imidazole derivatives are useful in treating inflammation, cerebral apoplexy, myocardial infarction, acute cardiac death,

cardiostenosis, and thrombus, and that benzene sulphonate is a pharmaceutically acceptable acid-addition salt.

158. The Laber patent refers to synergistic compositions (anti-microbial agents and antibiotics) (*See Testimony of Bradley Anderson, Trial Transcript VI, at 130.*) The third page of the Laber patent contains a boilerplate list of salts, which includes benzenesulphonate. *(Id. at 131.)*

159. The Laber patent teaches that compositions comprising a benzisothiazolinone derivative are a 2-nitrofuryl or 2-nitrothienyl derivative and are useful microbial agents. The patent discloses that "[t]he compounds . . . may be employed in free base form or in the form of pharmaceutically acceptable acid-addition salts. Suitable acid-addition salts include organic acid salts, such as fumarate, tartrate, or benzenesulphonate, and mineral acid salts, such as the hydrochloride, hydrobromide or sulphate."

160. The Teijin patent pertains to 1,4 dihydropyridine derivatives and their pharmaceutically acceptable acid addition salts. The patent application lists inorganic acids, carboxylic acids and organic sulphonic acids. The patent application describes mineral acids as the preferred acid; benzenesulphonic acid is not a mineral acid. One might have discovered the Teijin reference because of the key word "antihypertensive action." However, the Teijin reference describes hydrochloride salts. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 212; MTX 645.)*

ii. Ordinary Skill in the Art

161. A person of ordinary skill in the art in this case would be a formulation scientist with at least a Bachelor of Science degree, or the equivalent thereof, in chemistry or pharmacy or a related discipline and some relevant experience in the development and formulation of pharmaceutical products. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 78.)*

162. The person of ordinary skill in the art would not have to have had expertise with synthesizing chemical compounds and would not have been able to predict whether organic reactions, such as the MAR, could occur when compounds are combined in the solid state.

163. Dr. Bradley Anderson obtained a Masters and Ph.D. in pharmaceutical chemistry from the University of Kansas in 1978. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 71.)* He is currently the H.B. Kostenbauder professor at the University of Kentucky in the Department of Pharmaceutical Sciences, College of Pharmacy, and also is an adjunct professor at the University of Utah. Between 1971 and 1974, Dr. Anderson worked as a quality control chemist at Cutter-Haver Lockhart, which was involved in the manufacturing and sale of pharmaceuticals for veterinarian use. In 1978, Dr. Anderson joined the Upjohn Company, where he was a member of the pharmacy research group, which was the group that was involved in drug development and drug formulation. Dr. Anderson currently teaches courses to professional students and graduate students.[6] In the professional program, he

[6] " 'Professional students' are pharmacy students training to become pharmacists or Pharm Ds. The 'graduate students are training for their Ph.D. in pharmaceutical (continued...)

participates in a course that involves dosage forms, solutions, solid state, and stability. In the graduate program, he teaches a full semester course on rate processes, which concerns itself with drug stability and drug degradation. He also teaches a hands-on analytical course, which addresses chromatography, HPLC, TLC, capillary electrophoresis, GS, etc. Dr. Anderson also has published over 100 scientific articles during his career. (*Id.* at 70-74.)

164. The Court found Dr. Anderson qualified as an expert in the fields of pharmaceutical sciences and physical organic chemistry. *(Id.* at 77.)

165. A person of ordinary skill in the art at the time of the invention of the claims of the '303 patent could not have predicted whether toxic degradants or reaction products would be produced by amlodipine besylate, or what their clinical structures and amounts would be, without making and testing the salt. *(Id.* at 89.)

166. As of the date of invention of the claims of the '303 patent, a person of ordinary skill in the art would have understood the '909 patent as teaching that maleate salts of the 1,4-dihydropyridine compounds disclosed and claimed in the '909 patent were preferred. *(Stip. Fact, ¶ 52.)*

167. A person of ordinary skill in the art at the time of the invention of the claims of the '303 patent could not have predicted whether a new combination of a chemical base and acid would form a salt that is crystalline and has reproducible stoichiometry. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 90.)*

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[6](...continued)
sciences." *(See Testimony of Bradley Anderson, Trial Transcript VI, at 73)*

168. A person of ordinary skill in the art at the time of the invention of the claims of the '303 patent would have known of the MAR, but would not have expected it to occur in the solid state. (*Id.* at 141).

169. There is no prior art reference that teaches one of ordinary skill in the art that the MAR would occur between amlodipine and maleic acid in the amlodipine maleate salt.

170. A person of ordinary skill in the art at the time of the invention of the claims of the '303 patent would not have been aware of literature that discussed the MAR in a solid state, *e.g.,* tablets and capsule formulation. Moreover, if they had an understanding of the reaction, a person of ordinary skill in the art in 1986 would not have expected it to occur in the solid state. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 143.)*

171. A person of ordinary skill in the art at the time of the invention of the claims of the '303 patent would not have been able to predict the solubility of a salt. *(See Testimony of Bradley Anderson, Trial Transcript Vol. VI, at 160.)*

172. A person of ordinary skill in the art at the time of the invention of the claims of the '303 patent would have known that besylate is a pharmaceutically acceptable acid addition salt.

iii. The Differences Between the Claimed Invention and the Prior Art

The '909 Patent

173. In the '909 patent no sulphonate salts are identified or mentioned. The '909 patent specifically describes the maleate salt of amlodipine. It does not specifically describe any other salts of amlodipine. Amlodipine besylate is not specifically described in the '909

patent nor does the '909 patent describe or suggest combining the besylate anion with any particular base cation to form a besylate salt.

174. A person of ordinary skill in the art would have understood that the '909 patent identifies twelve (12) acid anions, any of which could have been tried with any of the millions of biologically active compounds to try to make a suitable salt.

175. A person of ordinary skill in the art would have understood as of the time of the invention of the claims of the '303 patent that the term "pharmaceutically acceptable acid addition salts" in the '909 patent does not describe or suggest any particular chemical structure of a salt, nor does it describe a chemical genus.

176. The '909 patent does not describe the MAR nor does it describe the instability problems that Pfizer scientists encountered with amlodipine maleate in solid formulations.

177. All but one of the working examples of salts in the '909 patent are either the maleate salt or salts made with other carboxylic acids, of which group the maleate salt is a member. The remaining example is not a salt.

The Berge Article

178. The Berge article does not describe salts of biologically active compounds or the indications for which any such compounds may be used, but lists anions that had been used with other base compounds to make pharmaceutical salts.

179. The Berge article discloses that, as of 1974, only 4.16% of the drugs commercially marketed in the United States were sulphonic acids.

180. The Berge article discloses that, as of 1974, the besylate anion was rarely used to make drugs which were commercially marketed in the United States because it teaches that besylate was used only 0.25% of the time. Only two besylate salts had FDA approval as of 1974, atracurium besylate and mesoridazine besylate. *(Stip. Fact, ¶ 50.)*

181. The chemical structures and biological activities of atracurium and mesoridazine are vastly different from the chemical structure and biological activity of amlodipine. *(Stip. Fact, ¶ 50.)*

182. Neither atracurium nor mesoridazine is a 1,4-dihydropyridine. Neither compound is approved by the FDA for treating either hypertension or ischaemia.

183. Atracurium is a neuromuscular blocking agent used as an aid for anesthesia. Mesoridazine belongs to a class of compounds for antidepressants or antipsychotics. *(See Testimony of Bradley Anderson, Trial Transcript Vol. VI, at 116, 118.)*

The Tanouchi Patent

184. The Tanouchi patent lists examples only with inorganic salts. *(See PTX 514; Testimony of Bradley Anderson, Trial Transcript Vol. VI, at 135.)*

The Laber Patent

185. The chemical structures listed in the Laber patent neither relate in any way nor are similar in any way to the structure of amlodipine. The patent indicates that the preferred salts are hydrochlorides. There are no examples of benzenesulphonate salts listed in the patent. *(See PTX 512; Anderson Test., Vol. VI, at 131-32.)*

186. Neither Berge, Barth, Schmidt, Spiegel, Laber, nor Tanouchi describe amlodipine besylate. Each of these references describe salts that were made or could have been made from bases that are different, structurally and biologically, from amlodipine.

The Teijin Patent

187. The Teijin patent does not provide any examples of besylate salts. Rather, all the examples are hydrochloride salts.

iv. Motivation Provided by the Prior Art

188. A person of ordinary skill in the art who was aware of the compound amlodipine maleate in 1986 would not have considered amlodipine besylate to be an obvious modification of amlodipine maleate because (i) the maleate salt is listed as the preferred salt in the '909 patent; and (ii) beyond maleate, the '909 patent gives no particular direction or no particular guidance in terms of "all the universe of possible choices." *(Testimony of Bradley Anderson, Trial Transcript Vol. VI, at 104.)*

189. The '909 patent, the Berge article, nor the existence of atracurium besylate or mesoridazine besylate, either alone or in combination, would have motivated one of ordinary skill in formulation science art to make amlodipine besylate in 1986. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 117.)*

190. The Schmidt patent has nothing to do with salts in the solid state. Therefore, the Schmidt patent, together with the '909 patent and the Berge article, would not have motivated one of ordinary skill in the art as of April 1986 to make amlodipine besylate. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 125-26.)*

191. The Speigel patent either alone or taken together with the '909 patent and the Berge article would not have provided any motivation for one of ordinary skill in the art of pharmaceutical formulation science in 1986 to make the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript Vol. VI, at 123.)*

192. The Tanouchi patent, either alone or together with the '909 patent and the Berge article, would not have provided any motivation to one of ordinary skill in the art of pharmaceutical formulation science in 1986 to make the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 135.)*

193. The Laber patent, either alone or together with the '909 patent and the Berge article, would not have provided any motivation to one of ordinary skill in the art of pharmaceutical formulation science in 1986 to make the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 132.)*

194. The Teijin reference, either alone or together with the '909 patent and the Berge article, would not have provided any motivation to one of ordinary skill in the art of formulation science in 1986 to make the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript Vol. VI, at 129, 212.)*

v. Reasonable Expectation of Success

195. A person of ordinary skill in the art of formulation science in April of 1986 would not have had a reasonable expectation that an acid used to make a salt approved by the FDA would make a salt of the compound amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript , Vol. VI, at 101.*)

196. A person of ordinary skill in the art of formulation science in 1986 would not have been able to predict the properties of a salt formed by amlodipine in an acid other than maleate acid. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 106.*)

197. A person of ordinary skill in the art of formulation science in 1986 would not have expected that another salt existed that had better physicochemical properties than amlodipine maleate. *(See Testimony of Bradley Anderson, Trial Transcript, Vol. VI, at 110.*)

198. Even assuming that the physicochemical properties of amlodipine maleate were described in publicly available references as of April of 1986, a person of ordinary skill in the art would not have had any reasonable basis to expect that a salt having better properties than amlodipine maleate would exist. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 111.)*

199. A person of ordinary skill in the art of formulation science in 1986 would not have been able to predict that an acid anion listed by Berge would form a pharmaceutically acceptable acid addition salt with a particular drug base. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 115.)*

200. The '909 patent, the Berge article, and the existence of atracurium besylate or mesoridazine besylate, either alone or in combination, would not have provided a person of ordinary skill in the art of formulation science in 1986 with a reasonable expectation of success with respect to making amlodipine besylate because one cannot predict what the properties of a new salt will be. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 117.)*

201. The Schmidt patent, either alone or together with the '909 patent and the Berge article, would not have motivated one of ordinary skill in the art of formulation science

in April 1986 with a reasonable expectation of success with respect to amlodipine besylate. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 126.)*

202. The Spiegel patent either alone or together with the '909 patent and the Berge article would not have provided a person of ordinary skill in the art of formulation science in 1986 with a reasonable expectation of success with respect to amlodipine besylate. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 123.)*

203. The Tanouchi patent, either alone or together with the '909 patent and the Berge article, would not have provided a person of ordinary skill in the art in 1986 with a reasonable expectation of success with respect to the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 136.)*

204. The Laber patent, either alone or together with the '909 patent and the Berge article, would not have provided a person of ordinary skill in the art in 1986 with a reasonable expectation of success with respect to the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 133.)*

205. The Teijin patent, either alone or together with the '909 patent and the Berge article, would not have provided a person of ordinary skill in the art of formulation science in 1986 with any reasonable expectation of success with respect to the besylate salt of amlodipine. *(See Testimony of Bradley Anderson, Trial Transcript VI, at 130.)*

vi. Unexpected Superior Formulation Properties of Amlodipine Besylate

206. Amlodipine besylate exhibits good solubility. One of ordinary skill in the art as of the time of the invention of the claims of the '303 patent could not have predicted that amlodipine besylate would have good aqueous solubility without making and testing the solubility of amlodipine besylate.

207. Amlodipine besylate is nonhygroscopic over a wide range of temperatures, relative humidities, and times, and is the only sulphonic acid salt of amlodipine that was not hygroscopic. One of ordinary skill in the art as of the time of the invention of the claims of the '303 patent could not have predicted that amlodipine besylate would be nonhygroscopic over a wide range of temperatures, relative humidities, and times without making and testing the hygroscopicity of amlodipine besylate.

208. The formulation stability testing conducted by Pfizer demonstrated that the formulation stability of amlodipine besylate is better than amlodipine maleate.

209. One of ordinary skill in the art as of the time of the invention of the claims of the '303 patent could not have predicted that amlodipine besylate would exhibit chemical formulation stability that is superior to that of amlodipine maleate without making and testing the chemical formulation stability of amlodipine besylate.

210. Amlodipine besylate has good processability and is forty-one percent (41%) less sticky than the prior art amlodipine maleate salt.

211. One of ordinary skill in the art as of the time of the invention of the claims of the '303 patent could not have predicted that amlodipine besylate would have good processing

properties which are superior to those of amlodipine maleate without making and testing the processability of amlodipine besylate.

212. It was not predictable as of the time of the invention of the claims of the '303 patent, that one salt of amlodipine would have advantageous properties in each of the physicochemical categories of solubility, hygroscopicity, stability, and processability without any significant disadvantages.

213. The besylate salt of amlodipine is superior to the prior art of amlodipine maleate because it has a superior combination of properties.

214. The superior properties of amlodipine besylate, individually and in combination, were unexpected at the time it was invented.

215. Amlodipine besylate's combination of advantageous formulation properties makes it highly suitable for use as an active drug compound in direct compression tablet formulations of amlodipine.

C. Inequitable Conduct

216. Mylan contends that Dr. Wells made six material misrepresentations and/or omissions with the intent to deceive the PTO in his Declaration to the PTO.

217. First, Mylan contends that the statement that the previously preferred maleate "has unacceptable stability characteristics" is a material misrepresentation because the statement was made with respect to both maleate tablets and capsules and there is no evidence which shows that the capsules had "unacceptable stability characteristics." In support of its

position, Mylan points out that at the time of the Wells Declaration, the maleate capsules were being used in live human clinical trials and their shelf life had increased.

218. In April of 1985, Dr. G. W. McLay reported concerns to Dr. C. A. P.D. Saxton, in Pfizer New York, about problems with the stability and processing of the amlodipine maleate capsules, especially with respect to suboptimal robustness of the maleate capsules ("although this formulation may be marketable its robustness in terms of processing and stability is not optimal."). *(See PTX 566.)* In that same memo, he stated "we may be able to market these, but they're not optimal and they have problems with stability and they're not robust because they're sticking to the dosators." *(Id.)*

219. Pfizer established through its testing and experimentation that amlodipine besylate is superior to amlodipine maleate, based on its superior stability and processability, and advantageous physicochemical properties. Pfizer concluded that amlodipine besylate tablets are superior to amlodipine maleate tablets.

220. Pfizer concluded that the capsule formulation that was most stable had the Mannitol; however, in Dr. Wells' memo of October 11, 1984, he describes that there is processing problems with that formulation because the Mannitol is sticking to the dosators. *See PTX 76.)*

221. Further in May 1985, Pfizer reported that it had processing and stability concerns with the clinical capsule formulations with the maleate salt, which indicated that a more robust formulation should be developed as a potential commercial product using the besylate salt because it was better in capsules than the maleate salt.

222. Such that, Dr. McLay reported that "[w]e have concluded that the poor stability of amlodipine maleate tablet formulation preclude their commercialization." *(See PTX 566.*)

223. Second, Mylan contends that Dr. Wells did not tell the PTO about the experiments Pfizer had conducted with the amlodipine maleate tablet using two percent (2%) magnesium stearate, which solved the sticking problem. *(See PTX 77 / MTX 323 - Figure 3.*)

224. The experiment reflected in Figure 3 is a comparative study which Mr. Davison ran in order to decide how much lubricant to put in his tableting mix to do the study. Mr. Davison testified that he wanted to determine how these salts relate to each other in stickiness. If he puts too much magnesium stearate in the formulation, none of the compounds would stick. Figure 3 deals only with amlodipine maleate. *(See Depo. of Edward Davison, Pfizer v. Apotex, at 113.)* This was not an experiment to evaluate the level of magnesium stearate which would avoid punch-filming in commercial-sized runs of amlodipine maleate tablets, but, rather, to determine the level of magnesium stearate that allows one to tell the difference between the salts and their natural properties while allowing one to run the tableting machine in order to conduct the test.

225. Figure 3 was not given to the PTO because it was not relevant or material to anything the PTO was asked to decide in the '303 patent prosecution. It provides no information regarding the relative stickiness of the seven amlodipine salts tested.. Dr. Wells told the PTO that besylate was superior in that it was much less adherent (sticky) than the maleate. Whether stickiness in the maleate tablets could be eliminated with two percent (2%) of a lubricant was not material or relevant to the actual issue before the PTO.

226. Third, Mylan contends that Dr. Wells did not tell the PTO about the drug loading experiments Pfizer had conducted using amlodipine maleate in two percent (2%) Avicel which produced a "spectacularly flat and highly acceptable" level of stickiness. (*See PTX 77 / MTX 323 - Figure 5.)*

227. Like the Figure 3 experiment, the Figure 5 experiment was a control experiment. The test measured for one salt (amlodipine maleate) the effect of drug loading on sticking. The purpose of the test was to determine a level of drug loading which would permit the observation and measurement of differences in stickiness of the various amlodipine salts.

228. The Figure 5 experiment is not relevant or material to the '303 patent prosecution insofar as it provides no information regarding the relative stickiness of the seven amlodipine salts tested.

229. Fourth, Mylan contends that Dr. Wells submitted a punch-filming test to the PTO which was "irrelevant [and] . . . meaningless" because it did not contain a lubricant. *(See PTX 77 / MTX 323 - Figure 7.)*

230. Fifth, in the alternative, Mylan contends that if in fact a lubricant was used in the punch-filming test, then the patent is wrong, the application is wrong, and the Wells Declaration is wrong because none of those documents reference a lubricant in the amlodipine besylate formulation.

231. Undeniably, during the instant trial, Dr. Wells changed his previous testimony and now testified that the punch-filming test did in fact contain a lubricant. He explained that he was wrong when he previously stated that no lubricant was used. Since his prior testimony in various depositions and at the Apotex trial, Dr, Wells has had the occasion to

review the Studies on Drug Sticking (Punch Filming) Report *(PTX 77 / MTX 323)* in detail and realized that his prior testimony that no lubricant was used was incorrect. The Court finds Dr. Wells' testimony at trial to have been credible.

232. Significantly, Mr. Davison, the scientist who actually conducted the experiments, has consistently and unequivocally maintained that he ran the formulation tests with magnesium stearate as the lubricant. *See Depo. of Davison, at 163* ("It would be highly surprising of me to run a tablet blend with no lubricant in it on a tablet, instrumented tablet press. I mean, it would be looked at as professional incompetent . . . .") Further, the report itself indicates over and over again that the experiments were conducted using magnesium stearate as the lubricant. It is clear that magnesium stearate was used in the test because one would not do an experiment (Figure 3) to determine an appropriate level of magnesium stearate if one were not going to use magnesium stearate in the ultimate test formulation.

233. Lastly, Mylan contends that Dr. Wells misrepresented to the PTO the pH of the amlodipine besylate. In his Declaration, Dr. Wells made the representation that salts which provide solutions having a pH close to that of blood (7.4 pH) are preferred.

234. In October, 1984, Dr. Wells listed the pH of besylate as 4.5 (*see MTX130, at P0152406*); in the patent application the pH of besylate is shown as 6.6; and in a May 1986 memorandum written by Dr. Wells, the pH of besylate is again listed as 4.5. (S*ee MTX 646, at A15289.*)

235. Experts for both Pfizer and Mylan agree that the difference between a 4.5 pH and 6.6 pH is scientifically not material.

236. Dr. Anderson testified that the pH of a salt can easily vary such that these minor differences in pH are of no material significance. Essentially this is a normal variation.

237. All of the problems which developed with the stability and processability of amlodipine maleate arose years before the '303 application. There is no evidence that shows any reference to the thought of applying for a patent application for amlodipine besylate until well after the problems with the maleate salt were discovered and the overall superiority of amlodipine besylate was established.

CONCLUSIONS OF LAW

1. To the extent any of the foregoing findings of fact is a conclusion of law, it is hereby adopted as a conclusion of law. To the extent any of the following conclusions of law is a finding of fact, it is hereby adopted as a finding of fact.

I. Controlling Authority

A. Jurisdiction

2. The court has subject matter jurisdiction over this case pursuant to 28 U.S.C. §§ 1391 and 1338(a).

3. Venue is proper in this district under 28 U.S.C. § 1400(b).

4. This Court has personal jurisdiction over the defendants Mylan Laboratories Inc. and Mylan Pharmaceuticals, Inc.

5. The 1984 Hatch-Waxman amendments to the Federal Food, Drug, and Cosmetic Act regulate the process by which generic drug companies gain approval from the FDA to bring generic pharmaceuticals to market. *21 U.S.C. § 355.*

6. The filing of an application with the FDA under 21 U.S.C. § 355 for a drug claimed in a patent or the use of which is claimed in a patent is an act of patent infringement if the intention of the applicant is the commercial manufacture, use, or sale of the drug before the patent expires. *35 U.S.C. § 271(e)(2)(A).*

7. An applicant must make a certification with respect to the patents that cover the generic drug product which is the subject of the application that the ANDA will not infringe the patents or that the patents are invalid. *21 U.S.C. § 355(j)(2)(A)(vii)(IV).*

8. Upon receiving notice of the applicant's certification regarding the patents, the patent holder may bring an action in the United States District Court for a declaration of whether the applicant will infringe the patent. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1570-71 (Fed. Cir. 1997).

B. Federal Circuit Law Applies

9. Any appeal in this action, which arises under the patent laws of the United States, must be to the United States Court of Appeals for the Federal Circuit, 28 U.S.C. § 1295(a), whose precedent governs matters of substantive patent law in this Court. The Federal Circuit has adopted decisions of the Court of Customs and Patent Appeals ("C.C.P.A.") as its own precedent, making those decisions binding on this Court. *E.g., Southwire Co. v. Essex Group, Inc.*, 220 U.S.P.Q. 1053, 1056 n.6 (N.D. Ill. 1983) ("The law that controls this action . .

. is the law of the Federal Circuit [, which] has declared that the patent decisions of [the C.C.P.A.] will be considered binding . . . . ") (*citing South Corp. v. United States*, 690 F.2d 1368, 1370 (Fed. Cir. 1982) (en banc)).

C. The Presumption of Validity

10. Issued patents have a strong presumption of validity in infringement proceedings. *35 U.S.C. § 282.*

11. The party asserting the invalidity of a patent bears the burden to prove each element of invalidity by clear and convincing evidence. *Norian Corp. v. Stryker Corp.,* 363 F.3d 1321, 1326 (Fed. Cir. 2004); *Monarch Knitting Mach. Corp. v. Sulzer Morat GmgH*, 139 F.3d 877, 881 (Fed. Cir. 1998).

12. Each patent claim constitutes a separate invention and the validity of each claim must be considered separately. *Ortho Pharm. Corp. v. Smith*, 959 F.2d 936, 942 (Fed. Cir. 1992).

13. "Clear and convincing evidence exists when the movant 'place[s] in the mind of the ultimate fact finder an abiding conviction that the truth of its factual contentions are highly probable." *Teleflex v. KSR Intern. Co.*, 119 Fed. Appx. 282, 285 (Fed. Cir. 2005), *cert. granted,* -- U.S. --, 126 S. Ct. 2965 (June 26, 2006) (*quoting Colorado v. New Mexico,* 467 U.S. 310, 316 (1984)).[7]

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[7] On June 26, 2006, the United States Supreme Court granted certiorari in *Teleflex, Inc. v.. KSR Int. Co.,* 119 Fed. Appx. 282 (Fed. Cir. 2005), *cert. granted,* 126 S. Ct. 2965 (2006), and on November 27, 2006, while the instant matter was being tried, the Supreme Court heard oral arguments in the *Teleflex* case, which may put in

(continued...)

14. It is more difficult to overcome the presumption of validity and meet the burden of proof by clear and convincing evidence when the references relied on in support of the validity challenge were before the patent office examiner at the time the patent issued. *Am. Hoist & Derrick Co. v. Sowa and Sons, Inc*., 725 F.2d 1350, 1358 (Fed. Cir.), *cert. denied*, 469 U.S. 821 (1984).

II. The Validity of the '303 Patent

15. The nonobviousness requirement is set forth in 35 U.S.C. § 103(a) (" § 103"), and reads:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. § 103(a)). *See also Graham v. John Deere Co.,* 383 U.S. 1, 14 (1966).

16. Although the determination of obviousness is ultimately a legal conclusion, it rests on underlying factual determinations. *See Graham*, 383 U.S. at 17-18.

17. These factual elements are: (i) the scope and content of the prior art; (ii) the difference between the prior art and the claims at issue; (iii) the level of ordinary skill in the

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[7] (...continued)
question the continuing vitality of the Federal Circuit's jurisprudence regarding the concept of obviousness. Nevertheless, the Court has tried to analyze the obviousness claim in a manner faithful to current Federal Circuit jurisprudence, including that found in *Teleflex*.

pertinent art; and (iv) objective or secondary considerations, such as whether there was a long-felt but unresolved need for the claimed invention, the failure of others, or whether the invention has enjoyed commercial success. *Id.*; *Alza Corp. v. Mylan Labs., Inc.,* 464 F.3d 1286, 1290 (Fed. Cir. 2006).

18. The claimed invention must be viewed " in the state of the art that existed at the time the invention was made." *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1050-51 (Fed. Cir.), *cert. denied*, 488 U.S. 825 (1988); see also *Al-Site Corp. v. VSI Intern., Inc.*, 174 F.3d 1308, 1323 (Fed. Cir. 1999).

19. In order to establish a *prima facie* case of obviousness, the party challenging the patent must prove by clear and convincing evidence that: (i) there was a suggestion or motivation in the prior art that would motivate one of ordinary skill in the art to make the claimed invention; and (b) that a person of ordinary skill in the art would have had a reasonable expectation that the invention would be successful at the time the invention was made. *See In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991); *Kaufman Co., Inc. v. Lantech, Inc.,* 807 F.2d 970, 974-75 (Fed. Cir. 1986); *Yamanouchi Pharm. Co. v. Danbury Pharm.,* 231 F.3d 1339, 1343 (Fed. Cir. 2000).

20. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau,* 353 F.2d 238, 241 (C.C.P.A 1965).

21. What a reference teaches is a question of fact addressed to a "person of ordinary skill in the art." *In re Bell*, 991 F.2d 781, 784 (Fed. Cir. 1993). The person of ordinary

skill in the art is an objective legal construct who is presumed to be aware of all the relevant prior art. *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 963 (Fed. Cir. 1986). This person of ordinary skill in the art is not deemed to be an innovator; rather, he is "presumed to think along the lines of conventional wisdom in the art." *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985).

22. The motivation to combine references and reasonable expectation of success are also questions of fact. *Alza Corp. v. Mylan Labs., Inc.,* 464 F.3d 1286, 1290 (Fed. Cir. 2006).

23. "The motivation need not be found in the references sought to be combined, but may be found in any number of sources, including common knowledge, the prior art as a whole, or the nature of the problem itself." *DyStar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006); *Brown & Williamson Tobacco Corp. v. Phillip Morris Inc*., 229 F.3d 1120, 1125 (Fed. Cir. 2000).

24. In the context of the structural similarity between the claimed chemical compound and the prior art chemical compound(s), the prior art must give, *inter alia*, reason or motivation to make the claimed compound. *See In re Baird,* 16 F.3d 380 (Fed. Cir.1994) (holding that obviousness had not been shown based on a single reference because the PTO had not demonstrated motivation to select claimed species from prior genus of millions of compounds); *see also In re Dillon,* 919 F.2d 688, 692 (Fed. Cir.1990) (en banc) ("structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness . . . ."), *cert. denied*, 500 U.S. 904 (1991).

25. "[T]here is no requirement that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." *DyStar*, 464 F.3d at 1361 (*quoting Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1472 (Fed. Cir. 1997)).

26. The prior art must also provide a reasonable expectation of success. *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp*., 320 F.3d 1339, 1354 (Fed. Cir. 2003) ("A showing of obviousness requires a motivation or suggestion to combine or modify prior art references, coupled with a reasonable expectation of success. . . ."); *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed .Cir. 1988). "Obvious to try" is not sufficient. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986).

27. The assessment of obviousness also requires examination of objective evidence of nonobviousness. Such objective evidence, when present, must be considered and includes the extent of commercial success of the patented invention, unexpected properties of the invention compared to the prior art, whether the invention satisfies a long-felt need, whether others have failed to find a solution to the problem plaguing the art, and any copying of the invention by others. *Graham*, 383 U.S. at 17-18. The commercial success of a patented product supports the nonobviousness of a patent only where there is a nexus between the patent and the commercial success of the product patented. *Ormco Corp. v. Align Tech., Inc*., 463 F.3d 1299, 1311-12 (Fed. Cir. 2006).

28. Evidence of unexpected results are but a part of the "totality of the evidence" that is used to reach the ultimate conclusion of obviousness. *Richardson-Vicks Inc. v. The*

Upjohn Co., 122 F.3d 1476, 1483 (Fed. Cir. 1997). "The existence of such evidence, however, does not control the obviousness determination." *Id.*

29. Objective evidence is "often the most probative and cogent evidence in the record." *Stratoflex, Inc. v. Aeroquip Corp,* 713 F.2d 1530, 1538 (Fed. Cir 1983). "It may often establish that an invention appearing to have been obvious in light of the prior art was not. It is to be considered as part of all the evidence, not just when the decisionmaker remains in doubt after reviewing the art." *Id.* at 1538-39.

30. The party alleging obviousnesss has the burden of proof with respect to all of the obviousness factors, including, where relevant, objective evidence of nonobviousness. *See Dennison Mfg Co. v. Panduit Corp*., 475 U.S. 809, 810 (1986).

31. In *Teleflex,* the Federal Circuit Court held that:

> [w]hen obviousness is based on the teachings of multiple prior art references, the movant must also establish some "suggestion, teaching, or motivation" that would have led a person of ordinary skill in the art to combine prior art teachings in the manner claimed.

Teleflex, supra at 285 (internal citations omitted).

32. Once a *prima facie* case has been established, the burden shifts to the patentee to go forward with rebuttal evidence showing facts supporting nonobviousness. *Yamanouchi Pharm.,* 231 F.3d at 1343. Each fact forming the factual foundation upon which the Court bases its ultimate conclusion regarding the obviousness of the claimed subject matter as a whole must be established by clear and convincing evidence. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc*., 776 F.2d 281, 291-92 (Fed. Cir. 1985) (internal citations omitted).

33. A result is unexpected for the purpose of showing non-obviousness when the result could not have been predicted by a person of ordinary skill in the art at the time of the invention. *See In re May*, 574 F.2d 1082, 1094 (C.C.P.A. 1978).

34. In this case, the Court finds that the unexpected superior properties of the besylate salt of amlodipine (*i.e.,* solubility, stability, hygroscopicity, and processability), compared to the prior art maleate salt of amlodipine are sufficient to overcome any potential case of *prima facie* obviousness. *See Glaxo Group Ltd. v. Apotex, Inc*., 376 F.3d 1339, 1349 (Fed. Cir. 2004).

35. As explained below, Mylan has failed to establish by clear and convincing evidence that the subject matter of any of claims 1, 2, and 3 of the '303 patent would have been obvious within the meaning of § 103 to a person of ordinary skill in the art as of April 4, 1986.

A. The Selection of The Besylate Salt Would Not Have Been Obvious

36. Mylan contends that the prior art, including the '909 patent, would have motivated a person of ordinary skill in the art to make amlodipine besylate. To prevail on its theory that amlodipine besylate was obvious, Mylan must establish by clear and convincing evidence that one of ordinary skill in the art would have been motivated to select the besylate salt. *Yamanouchi,* 231 F.3d at 1344; *see also Dillon*, 919 F.2d at 692 (finding that *prima facie* obviousness is established "where the prior art gives reason or motivation to make the claimed compositions").

37. The Court concludes that Mylan has failed to show by clear and convincing evidence a motivation to create the besylate salt of amlodipine as contained in the prior art.

The '909 patent specifically directed that the maleate salt was the preferred salt. The '909 patent listed a number of other classes of acid(s) to try, none of which were sulphonates, of which benzene sulphonic acid is a member. None of the other prior art references provide a suggestion to combine amlodipine and benzene sulphonic acid in particular. Importantly, the prior art does not teach a reason for one skilled in the art to even try to improve upon the maleate salt.

38. Therefore, the Court finds and rules that Mylan has failed to show, by clear and convincing evidence, that one skilled in the art would have been motivated to create amlodipine besylate based solely upon a reading of the prior art.

B. There Was No Reasonable Expectation of Success

39. Moreover, Mylan has failed to prove by clear and convincing evidence that a person of ordinary skill in the art would have had a reasonable expectation that amlodipine besylate would be successful based on the '909 patent considered in combination with the Berge, Barth, Spiegel, Schmidt, Laber, Tanouchi references, or any other reference. *See Boehringer,* 320 F.3d at 1354.

40. Mylan has failed to prove by clear and convincing evidence that a person of ordinary skill in the art would have had a reasonable expectation that amlodipine besylate would be successful based on the knowledge that besylate salts of biologically active compounds had been made or suggested for chemical structures different than amlodipine, such as the compounds described in the Berge, Barth, Spiegel, Schmidt, Laber, and Tanouchi references.

41. Based on the prior art in 1986, a person of ordinary skill in the art would not have had a reasonable expectation that amlodipine besylate would be superior over the prior art salt, amlodipine maleate, because it was completely unpredictable as to whether a salt would form, much less whether it would form a pharmaceutically acceptable addition salt.

42. For all these reasons, the Court finds that Mylan has failed to establish a *prima facie* case of obviousness by clear and convincing evidence.

C. Unexpected Superior Formulation Properties of Amlodipine Besylate

43. If claims are found to be *prima facie* obvious, the burden shifts to the patentee to come forward with evidence rebutting the finding. The rebuttal may consist of a showing that the claimed invention has an unexpected, superior property compared with the closest prior art. When the patentee comes forward with rebuttal evidence of non-obviousness, all of the evidence for and against obviousness must be evaluated and the burden of proof by clear and convincing evidence that the claims are obvious in light of all the evidence remains on the party challenging the patent. *Hybritech,* 802 F.2d at 1385.

44. Unexpected superior properties from an invention support the conclusion that the invention was not obvious to one of ordinary skill in the art. *In re Baxter Travenol Labs*, 952 F.2d 388, 392 (Fed. Cir. 1991).

45. In order for a showing of unexpected results to be probative of nonobviousness, such evidence must at least establish that: (i) there actually is a difference between the results obtained and those of the closest prior art, and (ii) the difference actually

obtained would not have been expected by one skilled in the art at the time of the invention. *In re Freeman*, 474 F.2d 1318, 1324 (C.C.P.A. 1973).

46. Assessment of the obviousness of a chemical compound cannot, however, be based merely on comparisons between that compound's chemical structure and structures in the prior art. *In re Papesch,* 315 F.2d 381, 391 (C.C.P.A. 1963). The law of § 103 also requires consideration of the respective biological and pharmacological properties of the claimed compound and those in the prior art before a final conclusion of obviousness can be reached. *Id.*

47. One unexpected property superior to the closest prior art is sufficient to overcome a case of *prima facie* obviousness. There is not a need that the invention be unexpectedly superior in all properties. *In re Chupp*, 816 F.2d 643, 647 (Fed. Cir. 1987).

48. A result is unexpected for the purpose of showing non-obviousness when the result could not have been predicted by a person of ordinary skill in the art at the time of the invention. *In re May,* 574 F.2d 1082, 1094-95 (C.C.P.A. 1978.)

49. In the alternative, assuming *arguendo* that a case of *prima facie* obviousness has been established by Mylan, the Court finds and rules that Pfizer has established that amlodipine besylate exhibits an unexpectedly superior combination of formulation properties sufficient to overcome any case of *prima facie* obviousness.

50. Amlodipine besylate was unexpectedly superior to amlodipine maleate in stability which was significant and of practical and important value.

51. Amlodipine besylate was unexpectedly superior to amlodipine maleate in processability which was significant of practical and important value.

52. Amlodipine besylate has a superior and unexpected combination of formulation properties in that it had no shortcomings in any of the essential qualities of solubility, hygroscopicity, stability, and processability. This combination of these highly desirable properties is important and of practical value to a pharmaceutical formulation scientist and to a pharmaceutical manufacturer.

53. The Court finds and rules that the superior combination of formulation properties of amlodipine besylate was unexpected and could not have been predicted.

D. Conclusion Regarding Obviousness

54. An analysis under *Graham,* which considers the scope and content of the prior art, the level of skill in the art, the differences between the prior art and the amlodipine besylate, and the objective evidence of nonobviousness, leads the Court to conclude that Mylan has failed to prove by clear and convincing evidence that the subject matter in claims 1, 2, and 3 of the '303 patent would have been obvious within the meaning of 35 U.S.C. § 103 to a person of ordinary skill in the art as of April 4, 1986, the filing date of the British priority application to which the '303 patent is entitled under 35 U.S.C. § 119.

In the alternative, assuming *arguendo* that a *prima facie* case of obviousness was established by clear and convincing evidence, the Court finds and rules that Pfizer has established that amlodipine besylate exhibits an unexpectedly superior combination of formulation properties sufficient to overcome any case of *prima facie* obviousness.

III. Inequitable Conduct

55. Patent applicants have a duty to prosecute patents in the PTO with candor and good faith, including the duty to disclose information known to the applicants to be material to patentability. *37 C.F.R. § 1.56(a); see also Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1178 (Fed. Cir. 1995). "[I]nequitable conduct includes affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive." *Semiconductor Energy Lab. v. Samsung Electronics Co., Ltd.*, 204 F.3d 1368, 1373 (Fed. Cir. 2000), *cert. denied*, 531 U.S. 1190 (2001); *Molins,* 48 F.3d at 1178.

56. The duty of candor extends throughout the patent's entire prosecution history. *Baxter Int'l v. McGaw, Inc.*, 149 F.3d 1321, 1331 (Fed. Cir. 1998); *Fox Indus. v. Structural Preservation Sys., Inc.,* 922 F.2d 801, 803 (Fed. Cir. 1990).

57. If a patent applicant violates these duties, the patent may be held to be unenforceable due to inequitable conduct. *See Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226, 1233 (Fed. Cir. 2003).

58. A party who asserts that a patent is unenforceable due to inequitable conduct must prove materiality and intent by clear and convincing evidence. *Manville Sales Corp. v. Paramount Sys, Inc.,* 917 F.2d 544, 551 (Fed. Cir. 1990); *Kingsdown Med. Consultants, Ltd. v. Hollister, Inc.*, 863 F.2d 867, 872 (Fed. Cir. 1988).

59. "Inequitable conduct entails a two-step analysis: first, a determination of whether the withheld reference meets a threshold level of materiality and intent to mislead, and second, a weighing of the materiality and intent in light of all the circumstances to determine

whether the applicant's conduct is so culpable that the patent should be unenforceable." *GFI, Inc. v. Franklin Corp*., 265 F.3d 1268, 1273 (Fed. Cir. 2001); *see also Molins*, 48 F.3d at 1178.

60. This requires a careful balancing: when the misrepresentation or withheld information is highly material, a lesser quantum of proof is needed to establish the requisite intent. *See N.V. Akzo v. E.I. DuPont de Nemours*, 810 F.2d 1148, 1153 (Fed. Cir. 1987). In contrast, the less material the information, the greater the proof needed to establish a requisite intent must be. *Id.*

61. Thus, to prevail on its allegations of inequitable conduct, Mylan must prove that information that has allegedly been withheld or misrepresented was material to patentability. It must then demonstrate knowledge, chargeable to those responsible for prosecuting the application, of that information and of its materiality. Finally, it must prove that an individual (not "Pfizer" generally) having a duty of disclosure to the PTO, intentionally withheld or misrepresented the information with an intent to mislead the PTO.

A. Materiality

62. In evaluating materiality, the United States Federal Circuit Court has consistently referred to the standard set forth in Patent Trade Office Rule 56. *Bruno Indep. Living Aids, Inc., v. Acorn Mobility Servs., Ltd.*, 394 F.3d 1348, 1352 (Fed. Cir. 2005).

63. Prior to 1992, Rule 56 defined information as being material "where there is a substantial likelihood that a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent." *37 C.F.R. § 1.56.*

64. Because the '303 patent was filed prior to the date Rule 56 was amended, the Court must look to the pre-1992 version of the Rule.

65. A Declaration submitted to the PTO is highly material. *Ferring B.V. v. Barr Labs, Inc.*, 437 F.3d 1181, 1189 (Fed. Cir.), *cert. denied*, -- U.S. --, 127 S. Ct. 515 (2006).

66. A misrepresentation in a Declaration submitted to the PTO is *per se* material. *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1571 (Fed. Cir. 1983).

B. Intent to Deceive

67. The Federal Circuit has held that an actual intent to deceive is a required element. A good-faith error in judgment, a mistake, negligence, or even grossly negligent failures are not sufficient to render an otherwise valid patent unenforceable. *Kingsdown Medical Consultants, Ltd. v. Hollister, Inc*., 863 F.2d 867 (Fed. Cir. 1988).

68. Direct evidence of intent to deceive or mislead the PTO is "rarely available but may be inferred from clear and convincing evidence of the surrounding circumstances." *Baxter Int'l, Inc. v McGaw, Inc.,* 149 F.3d 1321, 1329 (Fed. Cir. 1998). "Generally, intent must be inferred from the facts and circumstances surrounding the applicant's conduct." *Molins*, 48 F.3d at 1180.

69. Intent to deceive, however, cannot be "inferred solely from the fact that information was not disclosed: there must be a factual basis for finding of deceptive intent." *Hebert v. Lisle Corp.*, 99 F.3d 1109, 1116 (Fed. Cir. 1996). "Although there may be special circumstances in which intent is appropriately deemed established by inference alone, there

must be sufficient evidence to support such inference." *Huff v. Siroflex of Am., Inc.,* 122 F.3d 1456, 1466 (Fed. Cir. 1997).

70. When determining whether intent has been shown, a court must consider the totality of the circumstances, including evidence of good faith. *Baxter,* 149 F.3d at 1330 ("It is the totality of the applicant's conduct that creates the inference upon which the applicant's intent can be ascertained.").

71. The required intent cannot be proven by evidence of materiality alone. "Inequitable conduct requires an intent to act inequitably. Materiality of an undisclosed reference does not presume an intent to deceive." *Halliburton Co. v. Schlumberger Tech. Corp*., 925 F.2d 1435, 1442 (Fed. Cir. 1991). "Intent is an independent element of inequitable conduct . . . and must be separately established." *Hupp,* 122 F.3d at 1465.

72. However, "[t]he more material the conduct, the less evidence of intent will be required in order to find that inequitable conduct has occurred." *PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc*., 225 F.3d 1315, 1319 (Fed. Cir. 2000).

73. A showing of subjective good faith militates against a finding of intent to deceive. *Kingsdown*, 863 F.2d at 876.

C. No One Associated With The Prosecution of the '303 Patent Committed Inequitable Conduct During The Prosecution of the '303 Patent

74. Mylan has failed to prove by clear and convincing evidence that anyone associated with the prosecution of the '303 patent purposefully misrepresented or concealed material information with an intent to deceive the PTO.

75. Mylan contends that Dr. Wells misrepresented the results of the sticking test run by Mr. Davison. However, this test depended on comparisons of the rate of accumulation of amlodipine salts on tablet punches, not on absolute amounts of salt stuck to the punch press. The Court finds and rules that there was no misstatement or non-disclosure by the applicants of any material fact with regard to the stickiness data.

76. The '303 patent does not state that the amlodipine besylate does not stick at all. It simply states that amlodipine besylate is forty-one percent (41%) less sticky than amlodipine maleate.

77. Mylan contends that the patent applicants misrepresented the solubility and pH values reported in the patent. However, the evidence adduced at trial demonstrated that solubility and pH values may vary from one measurement to another based on differences in the purity of the salt from batch-to-batch and from variations in procedures used to measure solubility and pH.

78. The Court finds and rules that the difference between the different solubility values of amlodipine besylate was not material, as all reported values far exceeded the threshold value(s) needed for good bioavailability.

79. Moreover, the patent applicants did not assert that amlodipine besylate had solubility or pH values that made it superior to amlodipine maleate or the new amlodipine salts tested.

80. Mylan failed to prove by clear and convincing evidence that Dr. Wells' made any material misrepresentations or omissions to the PTO. In addition, Mylan failed to prove by clear and convincing evidence, either directly or inferentially, that Dr. Wells acted with an

intent to deceive the PTO. *See Semiconductor Energy Lab.*, 204 F.3d at 1373 ("inequitable conduct includes affirmative misrepresentation of material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive.") (*quoting Molins*, 48 F.3d at 1178).

D. Conclusion Regarding Inequitable Conduct

81. Neither Dr. Wells, nor Mr. Davison, nor any person who substantively participated in the prosecution of the '303 patent made any misrepresentation of a material fact or failed to disclose a material fact to the PTO.

82. Neither Dr. Wells, nor Mr. Davison, nor any person who substantively participated in the prosecution of the '303 patent committed any acts during the prosecution of the '303 patent, or failed to take any action during the prosecution of the '303 patent, with an intent to deceive or mislead the PTO.

83. The Court finds and rules that Mylan has failed to prove by clear and convincing evidence any material misrepresentation or non-disclosure which would compel a finding of inequitable conduct.

84. Even if the Court had determined that Mylan had met its burdens of proof on the elements of materiality and intent for any of its arguments, the Court is vested with the discretion to balance the degree of materiality and degree of intent to make an equitable judgment as to whether the conduct was so culpable that the patent should be barred from enforcement. *Life Techs., Inc. v. Clontech Labs., Inc.*, 224 F.3d 1320, 1324 (Fed. Cir. 2000).

85. In this case, even if Mylan had proven the required elements, the degree of culpability of Pfizer's representatives would be ever so slight and thus not sufficient to convince this Court that the proper remedy would be to invalidate the '303 patent.

86. The totality of the evidence in this case demonstrates that Mylan has not proven by clear and convincing evidence that the '303 patent is unenforceable due to inequitable conduct on the part of the inventors or anyone at Pfizer.

IV. SUMMARY OF CONCLUSIONS

87. For the reasons hereinabove set forth, the Court find and rules that Mylan has failed to prove by clear and convincing evidence that claims 1, 2, and 3 of the '303 patent are invalid as obvious under 35 U.S.C. § 103. In the alternative, assuming arguendo, that the '303 patent claims are invalid based on *prima facie* obviousness, the Court finds and rules that Pfizer has established by clear and convincing evidence that amlodipine besylate exhibits an unexpectedly superior combination of formulation properties sufficient to overcome any case of *prima facie* obviousness.

88. Mylan has further failed to prove by clear and convincing evidence that the '303 patent is unenforceable for inequitable conduct.

89. Mylan has stipulated that if the '303 patent is valid and enforceable, then its actions constitute infringement. Therefore, Mylan's submission of its ANDA to the FDA is an act of infringement of claims 1, 2, and 3 the '303 patent. *24 U.S.C. § 271(e)(2)(A).*

90. Accordingly, the Court will enter Judgment in this matter in favor of Pfizer Inc. and an injunction will issue to prevent Mylan from making, using, selling, offering to sell, or

importing into the United States the Mylan Amlodipine Tablets described in ANDA No. 76-418 until after the expiration of the '303 patent term, as extended by the pediatric exclusivity period.

An appropriate Order and Judgment consistent with these Findings of Fact and Conclusions of Law will be filed contemporaneously herewith.

McVerry, J.

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF PENNSYLVANIA

PFIZER INC.,	)	
	)	
Plaintiff and	)	
Counterclaim Defendant,	)	
	)	
v.	)	02: 02cv1628
	)	
MYLAN LABORATORIES, INC. and	)	
MYLAN PHARMACEUTICALS, INC.,	)	
	)	
Defendants and	)	
Counterclaim Plaintiffs.	)	

ORDER OF COURT

AND NOW, this 27th day of February, 2007, in accordance with the foregoing Findings of Fact and Conclusions of Law, is it **ORDERED**, **ADJUDGED, AND DECREED** that judgment in this action is hereby entered in favor of Pfizer Inc. and against Mylan Laboratories, Inc. and Mylan Pharmaceuticals, Inc.

Mylan Laboratories, Inc. and Mylan Pharmaceuticals, Inc., are hereby permanently enjoined from making, using, selling, offering to sell, or importing into the United States the Mylan Amlodipine Tablets described in ANDA No. 76-418 until after the expiration of Pfizer's '303 patent term, as extended by the pediatric exclusivity period.

BY THE COURT:

s/Terrence F. McVerry, Judge
United States District Court

cc: All Counsel of Record